Synthetic Plant-Growth Modifiers. IV. 2–Methyl–4–chlorophenoxyacetyl Derivatives of Amino Acids[1]

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Introduction

In the past 10 years, phenomenal advances have been made in the regulation of plant growth by organic compounds including some now used as herbicides. The introduction of new chemicals, new weed-control techniques, such as pre-emergence treatment, and low gallonage application are among the most important recent developments in the use of organic compounds for weed control. It is estimated that losses caused by weeds on farms have now reached 5 billion dollars annually, and at present well over 30 million pounds alone of the phenoxy compounds, 2,4–dichloro, 2,4,5–trichloro-, and 2–methyl–4—chlorophenoxyacetic acids (2,4–D, 2,4,5–T and MCP) are being used for herbicidal purposes to help combat these losses (9). The most recent of these three compounds to appear on the market in this country as an active ingredient in herbicidal formulations is 2–methyl–4–chlorophenoxyacetic acid. The chief claim made for its use as a herbicide is that it is less injurious to certain grasses, cereal crops and legumes and more effective on certain weeds than 2,4–D. Fertig (4) concludes that MCP is slower in action and definitely less injurious to legumes, and Crafts (3) cites a number of investigators who have shown that MCP is more selective than 2,4–D, particularly where clover, flax and other crops having leaves hard to wet are concerned. High specificity of the compound is indicated by numerous reports in the literature; Robinson's (8), on the effectiveness of MCP in selective weed control, is one example. However, from recent recommendations (1), there appears to be some disagreement on the use of MCP, indicating need for further testing and experimentation with the compound and its derivatives. MCP as sold may contain up to 40% of impurities by weight, some of which, according to Hanser (6), may have toxic properties.

Although the mode of action of the halogenated phenoxyacetic acids is not fully understood, indications of the mechanism involved when plants utilize some 2,4–D derivatives have been obtained by the synthesis and testing of a number of *D*–, *L*–, and *DL*–amino acid derivatives of these compounds. It has been reported that compounds prepared at this Laboratory (11) of the N–(2,4–dichlorophenoxyacetyl)–*L*–amino acid type appear to possess plant-growth modifying activity of the same magnitude as 2,4–dichlorophenoxyacetic acid (10,11). The *DL*–derivatives of this series are approximately one half as active as the *L*–isomers (10).

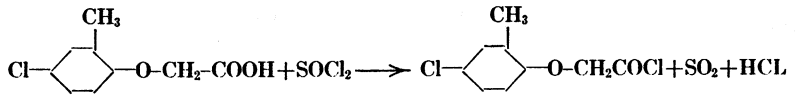
Plants affected by this type of growth-modifier appear to have cellular hydrolytic enzymes capable of splitting the amide linkage of *L*–amino acid compounds to liberate the free carboxyl group of the substituted phenoxyacetic acid which is deemed essential for activity. In the earlier investigation (11), the *D*–amino acid derivatives appeared to have little or no growth-modifying activity, suggesting that the assay plants were incapable of splitting the *D*–amide linkage; however, some of these *D*–amino acid derivatives did cause fruit to set and produced parthenocarpic fruit.

Because 2–methyl–4–chlorophenoxyacetic acid has important herbicidal properties and the amino acid derivatives of 2,4–D previously prepared (11) have been of particular value to investigators studying the mode of action of plant-growth modifiers (10), it was deemed advisable to prepare a series of MCP derivatives of the *D*–, *L*–, and *DL*–amino acid type. The new compounds prepared are listed in Table 1. Preliminary screening tests have been made, and a broad systematic herbicidal evaluation, including pre- and post-emergence tests, of the compounds is in progress.[2]

MCP Amino Acid Synthesis

The general procedure used for the preparation of the 2–methyl–4–chlorophenoxyacetyl derivatives is similar to the one described by Wood and Fontaine (11) for N–(2,4–dichlorophenoxyacetyl)–*D*–aspartic acid. The method is essentially the Schotten-Baumann reaction involving the use of the phenoxyacetyl chloride as intermediate. Modifications of the procedure are outlined under "Reaction Conditions". *Materials Used.* The 2–methyl–4–chlorophenoxyacetic acid used in this work was obtained from commercial sources[3] and further purified by recrystallization from benzene; m.p. 119°–120° C. The amino acids were the best obtainable from commercial sources and were used as received without further purification.

2–Methyl–4–chlorophenoxyacetyl chloride. This compound was prepared in 93.5% yield by the reaction of 2–methyl–4–chlorophenoxyacetic acid (I) (1 mole) with thionyl chloride (1.5 moles); the method used was essentially that described by Freed (5).



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[2]Herbicide tests being conducted by Dr. W. C. Shaw, Division of Weed Investigations, Bureau of Plant Industry, Soils, and Agricultural Engineering, Beltsville, Md.

[3]Supplied through the courtesy of Dow Chemical Company, Midland, Michigan and Monsanto Chemical Company, St. Louis, Missouri.

Table 1. Yields, physical properties and analyses of 2-methyl-4-chlorophenoxyacetylated amino acids.

N-(2-Methyl-4-chlorophenoxyacetyl)-	M.P., °C.[a] (Corr.)	Yield, %		Formulae	Analyses[b]					
					Cl		N		Optical rotation[c]	
		Crude	Refined		Calc'd.	Found	Calc'd.	Found	$[\alpha]_D^{25}$	Conc. (g./100 ml.) in pyridine
L-alanine	184.0–186.0	73.4	56.2	$C_{12}H_{14}ClNO_4$	13.05	13.00	5.15	5.13	+13.7±0.4	3.15
D-alanine	186.0–187.0	90.0	60.1		13.05	13.01	5.15	5.11	−13.5±0.4	3.04
DL-alanine	199.0–201.0	82.5	40.4		13.05	12.86	5.15	5.17		
L-aspartic acid	187.0–188.0[d]	56.8	34.8	$C_{13}H_{14}ClNO_6$	11.23	11.22	4.43	4.42	+42.5±0.5	2.52
D-aspartic acid	175.5–176.5	65.6	36.8		11.23	11.44	4.43	4.26	−41.2±0.5	2.63
DL-aspartic acid	203.0–205.0	37.8	22.4		11.23	11.34	4.43	4.44		
L-leucine	149.0–151.0	73.0	67.8	$C_{18}H_{20}ClNO_4$	11.30	11.31	4.46	4.44	+4.2±0.4	3.02
D-leucine	146.0–147.0	98.8	39.5		11.30	11.47	4.46	4.44	−4.3±0.4	3.10
DL-leucine	139.0–140.0	69.6	62.2		11.30	11.12	4.46	4.29		
L-methionine	123.0–124.0[e]	71.6	58.6	$C_{14}H_{18}ClNO_4S$	10.68	10.59	4.22	4.13	+10.3±0.4	3.03
D-methionine	124.0–125.0[e]	96.5	63.3		10.68	10.73	4.22	4.11	−8.6±0.4	3.12
DL-methionine	125.0–126.0	88.9	65.1		10.68	10.78	4.22	4.08		
L-phenylalanine	143.0–144.5	56.4	45.1	$C_{18}H_{18}ClNO_4$	10.19	10.25	4.03	4.08	+18.6±0.4[f]	3.02
D-phenylalanine	125.5–126.5	92.0	41.8		10.19	10.45	4.03	3.91	−24.1±0.4	3.78
DL-phenylalanine	132.0–133.0[g]	91.6	38.0		10.19	10.12	4.03	3.90		
L-threonine	108.5–110.0[h]	74.5	22.7	$C_{12}H_{16}ClNO_5$	11.75	11.57	4.64	4.53	+18.3±0.4	3.07
D-threonine	114.0–115.0[h]	70.6	26.5		11.75	11.69	4.64	4.54	−18.6±1.1	1.17
DL-threonine	144.5–145.5[i]	54.2	17.1		11.75	11.71	4.64	4.62		

[a]Recrystallized from 50% ethanol unless otherwise indicated.
[b]Analyses by M. J. Bythrow and R. B. Kelly.
[c]Optical rotations and interpretations by J. S. Ard.
[d]Required one additional recrystallization from ethyl acetate-petroleum ether.
[e]Required two additional recrystallizations, one from 25% ethanol, one from ethyl acetate-petroleum ether.
[f]Commercial *L*-phenylalanine used as an intermediate had a rotation in water of −29.2, as compared with the reported value of −34.5 (2) and of +34.5 determined for the commercial *D*-isomer used.
[g]Required two additional recrystallizations, one from 50% ethanol, one from 25% ethanol.
[h]No recrystallization from ethanol. Three from ethyl acetate-petroleum ether.
[i]Required four recrystallizations, two from 25% ethanol and two from ethyl acetate-petroleum ether.

The acid chloride (II) boiled at 70.0° C. at 0.005–0.008 mm., with constant index of refraction ($n_D^{32.8°}$) of 1.5400. It consisted of a colorless, super-cooled liquid which crystallized upon refrigeration.

N-(2-Methyl-4-chlorophenoxyacetyl)-L-leucine. The following description is included to illustrate in detail the general procedure employed in the synthesis of all the previously mentioned MCP amino acid derivatives. *L*-Leucine (III) (1.31 g., 0.010 M) was dissolved in 30 ml. of 1 *N* sodium hydroxide (0.030 M), and the mixture was chilled in an ice bath to 5° C. 2-Methyl-4-chlorophenoxyacetyl

chloride (2.15 g., 0.010 M) was dissolved in 8 ml. of benzene; the solution was chilled, and then added dropwise with mechanical stirring, over a 5 to 10-minute period, to the alkaline *L*-leucine solution (temperature maintained at 5° C.). The reaction mixture was stirred for 1 hour while it was allowed to warm up to room temperature and was then extracted once with a 40-ml. portion and three times with 10-ml. portions of ether in a separatory funnel. The ether fractions were combined and washed with 10 ml. of distilled water. The water washing of the ether fraction was added to the alkaline aqueous solution of the product. The alkaline solution was then neutralized with 1 *N* hydrochloric acid to pH 2. During the addition of hydrochloric acid a white crystalline precipitate began to appear at about pH 3.5–4. After cooling in the refrigerator for 1 hour, the N-(2-methyl-4-chlorophenoxyacetyl)-*L*-leucine (IV) was filtered off, slurried three times with water, filtered off after each slurry and finally left overnight in a vacuum desiccator, which was continuously evacuated by vacuum pump. The dried derivative was then washed three times with hot 10-ml. portions of petroleum ether (boiling range 63–70° C.). The crude yield was 2.29 g. (73.0%), m.p. 146–147° (Kofler micro melting point apparatus). The product dissolved in approximately 175 ml. of boiling 50% ethanol. After recrystallization, the yield was 2.13 g. (67.8%), m.p. 149–151°.

Reaction Conditions. The following modifications of the method of Wood and Fontaine (11) were used in the preparation of the 2-methyl-4-chlorophenoxyacetyl-amino acid derivatives:

The amino acids (0.010 to 0.020 molar) were dissolved in 3 mole-equivalents of alkali as described. Although chilling of the reaction mixture during addition of the 1 mole-equivalent of acid chlorides

was necessary, the stirring period at room temperature was reduced to 1 hour.

In all preparations except those involving threonine coupling, the crude acetylated derivatives separated as crystalline white solids. These were filtered off, washed with water, dried under vacuum at room temperature, thoroughly washed with hot petroleum ether (boiling range 63–70°C.), and recrystallized from 50% ethanol, with the exceptions noted in Table 1. All the threonine derivatives formed oils that failed to crystallize. Upon standing in the refrigerator, the oils changed to amorphous solids, which could be washed and treated in the manner described above. Each attempt to recrystallize a dried threonine derivative from ethanol-water solution resulted in formation of an oil. Crystalline products were obtained, however, from ethyl acetate-petroleum ether combinations, with ethyl acetate as the solvent and petroleum ether as the precipitant. This medium also gave a pure product with the other amino acid derivatives where difficulty was experienced in obtaining pure products by repeated recrystallizations from ethanol-water solutions.

All the dried crude products were thoroughly washed with hot petroleum ether to remove small amounts of 2–methyl–4–chlorophenoxyacetic acid.

Since the *D*– and *DL*–isomers of N–(2–methyl–4–chlorophenoxyacetyl)–aspartic acid underwent some decomposition during drying under vacuum at 50° C., all compounds were dried at room temperature to constant weight prior to chlorine and nitrogen analyses.

As shown by analysis, N–(2–methyl–4–chlorophenoxyacetyl)–*D*–methionine crystallized as a stable monohydrate. To obtain the analytical values for chlorine and nitrogen reported in Table 1, the sample was dried in a special charging tube in the manner described by Naghski et al. (7).

The "refined yield" percentage figures reported in Table 1 do not include additional quantities of products worked up from mother liquors.

Optical Rotations. In previous work with 2,4–D derivatives of amino acids (11), the rotations were determined in aqueous sodium hydroxide solution. When this medium was used for the present series of acids, the specific rotations in most cases seemed tolerably constant, but those of the N–(2–methyl–4–chlorophenoxyacetyl)–phenylalanine isomers changed drastically with concentration, and the values did not seem to be affected in the usual manner by impurities. Possibly this was caused by formation of micelles. Although such extreme effects were not observed for the other acids of this series, it did not seem advisable to use the aqueous sodium hydroxide medium. Specific rotations of the same acid were essentially constant with changing concentrations in pyridine, and the impurities in one isomer were revealed in the normal manner. Therefore, pyridine was selected as the medium for the rotation measurements reported in Table 1.

Preliminary Screening Tests

2–Methyl–4–chlorophenoxyacetyl derivatives of six amino acids (*D*–, *L*– and *DL*– forms), and the parent acid, were screened for plant-growth modifying properties by the following methods. Six different plants, namely, Pinto bean, Black Valentine bean, cucumber, sunflower, barley and corn were used.

Lanolin Methods:—In testing effects on bean plants, a paste was prepared by dissolving or mixing 12.5 mg. of the test compound in 0.25 gm. of Tween 20. One gm. of melted lanolin was then added and thoroughly mixed. The paste was applied as a band 3 – 5 mm. wide and about 1 mm. thick around the first internode midway between the first and second nodes of 3 young bean plants of each variety. This amounted to about 150 micrograms of the test compound per plant. At the time of treatment the plants had primary leaves about 1.25 inches in length. The trifoliate leaves were still tightly folded in the terminal buds.

In using sunflower and cucumber plants, the paste was applied as a band 2–4 mm. wide and about 1 mm. thick on the hypocotyls (immediately below the cotyledons) of 3 young cucumber plants, Arlington White Spine variety, and 3 young sunflower plants, small seeded type. At the time of treatment, both cucumber and sunflower plants had developed cotyledons that were fully almost expanded and about 1 inch in length. The first true leaves were still tightly folded in the terminal buds.

Coated Sand Method:—In using corn and barley plants, 32 mg. of the test compound was dissolved in or mixed with 0.4 ml. Tween 20; 6 ml. of 95% ethyl alcohol was added, and the mixture was stirred. Twenty grams of quartz sand were added to make a slurry, which was then dried at room temperature. Seeds of corn (U. S. 13 hybrid) and of barley (Wong) were planted separately in composted soil contained in 3-inch clay pots. Two pots of corn (4–6 seeds per pot) and two pots of barley (8–12 seeds per pot) were used in testing each compound. Two days after the seeds were planted, 5 gm. of the coated sand was sprinkled evenly over the surface of the soil in each pot. A thin layer of sifted soil was applied to hold the coated sand in place. This application rate was equivalent to 16 lbs. per acre.

At intervals of 2, 4, 6, and 14 days following treatment, the degree of growth modification induced by the various compounds was estimated and scored according to the intensity of growth responses. The following responses were taken into account: stem curvature, epinasty, formative effects, induced cellular proliferation (gall formation) and growth inhibition.

In Table 2 the scores for the 14th day's observations are recorded; to condense the data, the other scoring has been omitted. These data are representative, although they do not show the rate of response or relative progressive effectiveness of the compounds upon growth. The percentage of plants killed by the respective compounds is also listed, although such figures are not intended to reflect herbicidal potentialities of the compounds because the tests were not designed for

Table 2. Plant-growth modifying activity of 2-methyl-4-chlorophenoxyacetylated amino acids on Pinto Bean (PB), Black Valentine Bean (VB), Sunflower (S), Cucumber (C), Barley (B) and Corn (Cn).

N-(2-Methyl-4-chlorophenoxyacetyl)-	Lanolin Method[a]—14 Days After Treatment																							
	Stem curvature				Growth inhibition				Epinasty		Formative effects		Cell proliferation								Dead, %			
													First internode		Hypocotyl		Treated area							
	PB	*VB*	*S*	*C*	*PB*	*VB*	*S*	*C*	*S*	*C*	*VB*	*S*	*PB*	*VB*	*PB*	*VB*	*PB*	*VB*	*S*	*PB*	*VB*	*S*	*C*
Parent acid	+++	4+	4+	4+	++	4+	4+	4+	4+	4+	4+	4+	+++	4+	+++	4+			4+	0	100	100	100
L-alanine	+++	+++	4+	4+	++	+++	4+	4+	4+	4+	4+	4+	+++	+++	+++	+++			4+	0	50	100	100
D-alanine	+++	+++	4+	0	+	+++	4+	+	4+	4+	4+	4+	+++	+++	++	+++			4+	0	33	100	0
DL-alanine	+++	+++	4+	4+	+	+++	4+	4+	4+	4+	4+	4+	+++	+++	+	+++			4+	0	66	100	100
L-aspartic acid	+	4+	4+	4+	+	4+	4+	4+	4+	4+	4+	4+		4+		4+	+++	4+	4+	0	100	100	100
D-aspartic acid	0	++	++	++	++	++	++	+	0	+++	0+	+					+++	+++	4+	0	0	0	0
DL-aspartic acid	+	++	4+	+++	++	++	4+	++	4+	+++	4+	4+								0	0	100	0
L-leucine	+++	+++	4+	4+	++	+++	4+	4+	4+	4+	4+	4+	+++	+++	++	+++			4+	0	66	100	100
D-leucine	0	0	0	0	0	0	0	0	0	+	0	+	0	0	0	0	0	0	4+	0	0	0	0
DL-leucine	++	4+	4+	+++	+	4+	4+	+++	4+	+	4+	4+	++	4+	+	4+			4+	0	100	100	0
L-methionine	+++	4+	4+	4+	++	4+	4+	4+	4+	4+	4+	4+	+++	4+	+++	4+			4+	0	100	100	100
D-methionine	+	+++	+	++	+	+++	+	+++	+	0+	+	+	0	0	++	+++	0	0	4+	0	0	0	0
DL-methionine	+++	+++	4+	+++	+++	+++	4+	+++	4+	4+	4+	4+	+++	+++	++	+++			4+	0	33	100	0
L-phenylalanine	+++	+++	4+	4+	0	+++	4+	4+	4+	4+	4+	4+	+++	+++	+	+++			4+	0	0	100	100
D-phenylalanine	0	+++	4+	0	0	+++	4+	0	0	+++	0+	+					+++	+++	4+	0	0	0	0
DL-phenylalanine	0	++	4+	+++	0	++	4+	+++	4+	4+	4+	4+	+++	+++	+++	+++			4+	0	0	100	0
L-threonine	+++	+++	4+	4+	+	+++	4+	4+	4+	4+	4+	4+	+++	+++	+	+++			4+	0	0	100	100
D-threonine	0	++	++	++	0	++	++	+	0	+++	0+	+					+++	+++	4+	0	0	0	0
DL-threonine	++	+++	4+	4+	+	+++	4+	4+	4+	4+	4+	4+	+++	+++	++	+++			4+	0	0	100	0

[a]See text for method; 0, no effect; +, slight effect; ++, moderate effect; +++, marked effect; 4+, response could not be recorded because of inhibited growth or death of plants. These data represent the results of one complete experiment; at a later date the screening tests were repeated with essentially the same results.

Table 2 Continued. Plant-growth modifying activity of 2-methyl-4-chlorophenoxyacetylated amino acids on Pinto Bean (PB), Black Valentine Bean (VB), Sunflower (S), Cucumber (C), Barley (B) and Corn (Cn).

N-(2-Methyl-4-chlorophenoxyacetyl)-	Coated Sand Method[a]—14 Days After Treatment									
	Stem Curvature		Growth Inhibition		Formative Effects		Cell Proliferation Treated Area	
	B	*Cn*	*B*	*Cn*	*Cn*		*Cn*	
Parent acid	+++	++	++	++	++		++	
L-alanine	+++	+++	+++	+++	+++		+++	
D-alanine	+++	+ +	+++	+++	+ +		+++	
DL-alanine	+++	+++	+++	+++	+++		+++	
L-aspartic acid	++	+++	+++	+++				
D-aspartic acid	++	+++	+++	+++	+++		+++	
DL-aspartic acid	+++	+++	+++	+++	+++		+++	
L-leucine	+	+	+++	+++	+++		+++	
D-leucine	+	+	+++	+++	+++		+++	
DL-leucine	+	+++	+++	+++	+++		+++	
L-methionine	+		+++	+++	+		+++	
D-methionine	+++	+ +	+++	+++	++		+++	
DL-methionine	+++	+++	+++	+++	+++		+++	
L-phenylalanine	+	+	+++	+++	+		+++	
D-phenylalanine	+++	+++	+++	+++	+++		+++	
DL-phenylalanine		+	+++	+++				
L-threonine	+++	+ +	+++	+++	+		+++	
D-threonine	+++	+++	+++	+++	+		+++	
DL-threonine	+++	+++	+++	+++	+++		+++	

[a]See text for method; 0, no effect; +, slight effect; ++, moderate effect; +++, marked effect; 4+, response could not be recorded because of inhibited growth or death of plants. These data represent the results of one complete experiment; at a later date the screening tests were repeated with essentially the same results.

that purpose. Corn and barley plants were not killed in these tests.

The scores for the various responses to treatment with the *D*- and *L*-compounds were added, and an index value representing the percentage of maximum effectiveness based on 2, 4, 6 and 14 day observations was assigned to each compound. These index values are presented in Table 3. Index values of the *DL*-compounds have not been reported. The reason for this is that very high concentrations of each chemical were applied in order to illustrate all of the effects. At these high concentrations, the *DL*-compounds had index values comparable to the *L*-compounds.

Discussion of Results of Plant Screening Tests

Alanine Compounds:—The *D*-, *L*-, and *DL*-forms of 2-methyl-4-chlorophenoxyacetyl-alanine are about equally effective and possess moderate to strong growth-modifying properties, as shown by data in Table 2 and index values in Table 3; the *D*-alanine compound's action on cucumber is an exception to this statement. The *D*-form appears to have had little or no growth modifying effects on this plant during the 2-week observation period. The absence, or the presence of only a relatively small amount, of a hydrolytic enzyme capable of splitting the amide linkage of the *D*-amino acid deriva-

Table 3. Index values of growth-modifying properties of 2–methyl–4–chlorophenoxyacetyl derivatives of *D*– and *L*–amino acids.

Amino acid	Pinto Bean		Black Valentine Bean		Cucumber		Sunflower		Barley		Corn	
	D	L	D	L	D	L	D	L	D	L	D	L
Alanine	78*	94	94	94	5	90	67	70	42	42	93	93
Aspartic acid	44	39	33	94	62	90	52	59	33	67	60	93
Leucine	0	100	0	100	0	90	0	78	50	83	80	93
Methionine	39	100	61	100	67	90	26	56	42	42	80	93
Phenylalanine	0	72	0	100	0	90	0	67	33	42	67	93
Threonine	39	78	61	100	67	90	26	78	42	58	80	93
Parent acid	100		100		91		74		67		93	

*Index values (I.V.) represent calculated percentage of maximum effectiveness based on observed stem curvature, epinasty, cellular proliferation, formative effects and suppression of regulative growth at 2,4,6 and 14 days.

$$\text{I.V.} = \frac{\text{Summation of observed values for responses (2, 4, 6 and 14 days)} \times 100}{\text{Total number of observations (2, 4, 6 and 14 days)} \times 3 \text{ (max. rating)}}$$

tive is suggested as one of the possible reasons for this behavior. In barley, all three isomeric forms of alanine-MCP compounds seem to have somewhat limited effects on growth, with no killing action. The corn plant is somewhat more responsive to these compounds than barley; marked formative effects[4] were apparent but all plants survived the treatment. In some instances alanine compounds actually killed the plants, 100% of the sunflower and 33–50% of the Black Valentine bean; also *L*– and *DL*–alanine killed 100% of the cucumber.

Aspartic Acid, Methionine and Threonine Compounds:—All optical forms of these three amino acid compounds possess slight to marked influence upon growth responses (Tables 2 and 3). Generally, however, the *D*–isomer was not so effective as the *L*–form. In the case of the aspartic acid derivative, however, the response of the Pinto bean and sunflower to the *D*–isomer was essentially the same as that of the *L*–compound.

The Pinto bean (Table 3) gave a moderate response to *D*– and *L*–aspartic acid derivatives and the *D*–methionine and *D*–threonine derivatives. Cell proliferation occurred, however, at the area treated with both *D*–threonine–MCP compound and all forms of aspartic acid derivatives. These compounds induced a similar effect when applied to bean, sunflower and corn plants (Table 2). In general, the Black Valentine bean, the cucumber and the sunflower responded to a marked degree to the *L*–forms; all except *L*–threonine caused death of plants in every case. The *DL*–forms of aspartic acid-methionine- and threonine-MCP compounds were less effective. The *D*–forms of these three compounds never resulted in the death of any plant in the 2-week testing period. Barley was less responsive than corn to all optical forms of these three amino acid derivatives.

Leucine and Phenylalanine Compounds:—Differences in responses of plants treated with the *D*– and *L*–leucine and phenylalanine derivatives are most striking (Table 2). The Pinto and Black Valentine beans, cucumber and sunflower showed no response to the *D*–forms of these compounds. Growth inhibition and slight stem curvature occurred in the barley and corn plants, and the *D*–compounds had formative effects on corn. The *D*–isomers, however, did not produce death of plants during the test period. In these plants the amide linkage of the *D*–amino acid derivative appeared more difficult to hydrolyze than did that of the *L*–form. Behavior of the *L*– and *DL*–forms of leucine and phenylalanine was similar to that of the other amino acid *L*– and *DL*–forms previously described.

In these tests, the amino acid-MCP derivatives have shown marked selectivity depending on the kind of amino acid, the optical isomer, and the kind of plant.

[4]Unusual leaf shape.

Summary

A series of new 2–methyl–4–chlorophenoxyacetyl derivatives of *D*–, *L*–, and *DL*–amino acids was prepared, and the compounds were tested for plant-growth modifying activity.

In general, the derivatives of *DL*– and *L*–amino acids were active as plant-growth modifiers when tested on 6 different plants; those of *D*–amino acids were less active. The *D*–leucine and *D*–phenylalanine derivatives were inactive over the 2-week test period. Results varied in degree but were in close agreement with those previously reported for the behavior of some corresponding 2,4–dichlorophenoxyacetyl amino acids. The individual *D*–amino acid derivatives, exhibited a high degree of specificity and a wide variety and degree of activity relative to various plant responses.

Literature Cited

1. Baylor, J. E. Proceedings of Northeastern Weed Control Conference, Supplement 1953. Pp 13–15.
2. Birnbaum, S. M., Levintow, L., Kingsley, R. B., and Greenstein, J. P. J. Biol. Chem. *194*:455–470. 1952.
3. Crafts, A. S. Annual Review of Plant Physiology, *4*:253–282. 1953.
4. Fertig, S. N. Proceedings of Northeastern Weed Control Conference. 1952. Pp. 235–243.
5. Freed, V. H. J. Am. Chem. Soc. *68*:2112. 1946.
6. Hansen, B. Physiol. Plantarum *4*:667–676. 1951.
7. Naghski, J., Mellon, E. F., Korn, A. H., and Ogg, C. L. J. Am. Pharm. Assoc., Sci. Ed. *41*:599–602. 1952.
8. Robinson, B. P. Proceedings Southern Weed Control Conference. Pp. 192–193. 1953.
9. Shaw, W. C., and Lovvorn, R. L. Agricultural Chemicals *8*:32–35, 127–129, May 1953.
10. Weintraub, R. L. Journal of Agr. and Food Chem. *1*:250–254. 1953.
11. Wood, J. W., and Fontaine, T. D. J. Org. Chem. *17*:891–896. 1952.